

### **Remarks/Arguments**

Claims 1-5, 7-14, 20, 24 and 27 are pending. Claims 6 and 15-19 have been withdrawn. Claims 21-23, 25-26 and 28-47 have been cancelled without prejudice. Applicants reserve the right to pursue the subject matter of one or more of the cancelled claims in one or more related applications. Claims 1, 3, 8, 24, and 27 have been amended.

The subject matter encompassed by the amended claim is disclosed by the instant specification. Support for claims 1, 3, and 8 is on, *e.g.*, page 14, lines 3-9 of the instant specification. Support for claims 24 and 27 is in, *e.g.*, Example 7. Accordingly, no new matter has been added.

### **Rejections Under 35 U.S.C. § 112**

Claims 24 and 27 have been rejected under 35 U.S.C. § 112, second paragraph as being incomplete for omitting essential elements. The Examiner alleges that disclosure of how to cure a cell is an essential element of the claim yet the claim does not recite the steps required to obtain such a cell.

In the present case, one skilled in the art would understand what the claims refer to when reciting the term “cured cell” and that there are a number of ways to obtain such a cell by reading the specification. Applicants do not believe that reciting the steps of one particular method of curing a cell is essential to the claim. Applicants point out that the specification describes the characteristics of a cured cell as a cell that formerly contained a replicating replicon that does not currently contain a replicating replicon or detectable levels of replicon RNA (see, *e.g.*, page 31, lines 6-8 of the instant specification). Additionally, the specification discloses that there are a

number of different techniques that can be used for curing a cell (see, *e.g.*, page 19, lines 3-6 of the instant specification). The claims must "conform to the invention as set forth in the remainder of the specification and the terms and phrases used in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description." 37 CFR §1.75(d)(1).

Claim 13 has been rejected under 35 U.S.C. § 112, second paragraph as being incomplete for omitting essential elements. The Examiner alleges that the replicon must be within an expression vector in order to be transfected into cells yet such a requirement is not recited in the claim. Applicants disagree.

Applicants point out that *in vitro* transcribed replicon RNA (not in an expression vector) can be transfected into cells to produce replicon replication (see, *e.g.*, page 16, lines 19-22 of the instant specification). In fact, Applicants successfully used *in vitro* transcribed RNA to electroporate cells and were able to obtain replicon replication within the cells (see, *e.g.*, page 23, lines 19-23 and page 27, lines 15-18 and page 33, lines 23-24 of the instant specification). Accordingly, Applicants do not believe that having a replicon within an expression vector for cell transfection is essential.

Claims 24 and 27 have been rejected under 35 U.S.C. § 112, first paragraph because the specification does not enable a person skilled in the art to make and use the invention commensurate in scope with the claims. The Examiner contends that the specification is enabled for making a replicon enhanced cell *in vitro*. However, the Examiner alleges that *in vivo*

methods of making replicon enhanced cells are not enabled. Without admitting that the Examiner's characterization is valid, Applicants have amended claims 24 and 27 such that it is clear that *in vitro* methods only are encompassed.

In view of the foregoing, Applicants respectfully request withdrawal of the rejections under §112.

### **Rejection Under 35 U.S.C. § 103**

Claims 1, 2, 12 and 13 have been rejected under 35 U.S.C. § 103 as being obvious over Lohmann et al., 1999, Science 285:110-113 (hereafter "Lohmann") or Blight et al., 2000, Science 290:1972-1974 (hereafter "Blight") in view of Lanford et al., 2001, J. Virol. 75:8074-8081 (hereafter "Lanford"), Khromykh et al., 1997, J. Virol. 71:1497-1505 (hereafter "Khromykh") and Hong et al., US Patent Publication 2001/0034019 (hereafter "Hong"). Applicants respectfully disagree.

The Examiner points out that the art teaches HCV replicons (*e.g.*, Lohmann and Blight) and the existence of subgenomic replicons for other viruses including the Kunjin flavivirus (*e.g.*, Khromykh). According to the Examiner, Lanford allegedly provides the motivation to combine the disclosures *supra*. The Examiner contends it would have been obvious to one skilled in the art to make replicons using GBV.

The Examiner appreciates that Lohmann, Blight, and Khromykh do not mention GBV in any context or the desirability of making GBV replicons. However, according to the Examiner, Lanford discloses GBV as a model for HCV antiviral studies thereby motivating one skilled in the art to apply the teachings of Lohmann and Blight in connection with HCV to GBV.

Applicants point out that Lanford states that an HCV replicon system “cannot replace the need for a virus-based culture system and small-animal model” (see page 8074, right hand column, lines 17-20 of Lanford). One skilled in the art would not read that disclosure and be motivated to make a GBV replicon system as the Examiner alleges. According to Lanford, an HCV replicon system is less desirable than a GBV full length virus based system for HCV antiviral studies. This disclosure would not lead someone to develop a GBV replicon system for HCV antiviral studies.

Hong discloses chimeric full length viruses with a GBV genome that has been modified by replacing a non-structural gene with the analogous gene from HCV (see, *e.g.*, paragraph 0029, lines 1-8). There no disclosure of any replicons. Similarly, there is no disclosure of a replicon or virus containing GBV non-structural genes because at least one of those genes is an HCV equivalent in Hong’s disclosed constructs (see, *e.g.*, paragraph 0057 of Hong).

The principle that the prior art must contain a suggestion of the desirability of the proposed combination of isolated disclosures in order to render an invention obvious has been espoused by the United States Court of Customs and Patent Appeals in *Application of Bergel*, 292 F.2d 955, 130 U.S.P.Q. 206 (C.C.P.A. 1961) and was reaffirmed by the Court of Appeals for the Federal Circuit in *In re Sernaker*, 702 F.2d 989, 217 U.S.P.Q. 1 (Fed. Cir. 1983) and in *In re Grabiak*, 769 F.2d 729, 226 U.S.P.Q. 870 (Fed. Cir. 1985). Applicants submit that there is no motivation or suggestion to apply the teachings of replicons of Lohmann, Blight or Khromykh to GBV or to combine it with the teachings of full length viruses of Lanford or Hong. Furthermore, Applicants believe that the Examiner has impermissibly used hindsight to read

Applicant's disclosure into the art to arrive at the invention. See *In re Pleuddeman*, 15 U.S.P.Q. 2d 1738 (Fed. Cir. 1990).

In view of the foregoing, Applicants respectfully request withdrawal of the rejection under §103.

**Conclusion**

It is believed that the claims now pending are in condition for allowance. Early and favorable action by the Examiner is earnestly requested.


**Authorization**

The Commissioner is hereby authorized to charge any fees which may be required for consideration of this Amendment to deposit account 13-2755.

Respectfully submitted,

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By:



Melissa B. Wenk

Reg. No. 53,759

Attorney for Applicants

**Correspondence Address:**

Merck & Co., Inc.

P.O. Box 2000

Rahway, NJ 07065-0907

(732) 594-2756 Telephone

(732) 594-7790 Facsimile